## REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-14 are in this case. Claims 9-14 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claim 2 was previously cancelled.

### *35 U.S.C. § 103 Rejections*

The Examiner has rejected claims 1, 3, 4, 7 and 8 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 4,469,676 in view of Brittberg *et al.* (NEJM 331: 889-895, 1994).

The Examiner points out that U.S. Pat. No. 4,469,676 teaches a method of treating wrinkles by injecting non-isolated cartilage cells into the wrinkles. The Examiner also points out that Brittberg *et al.* teach that isolated chondrocytes can be administered via injection to produce cartilage at the injected site for use in reconstructive surgery. The Examiner asserts that an ordinary person skilled in the art would reasonably expect that isolated chondrocytes would be successfully used in place of the non-isolate cartilage cells of U.S. Pat. No. 4,469,676 and therefore would have been motivated to treat wrinkles by subcutaneously injecting chondrocytes into the site of the wrinkles.

Applicant wishes to point out that U.S. Pat. No. 4,469,676 teaches use of a cosmetic filler which consists of sterile tissue (biologically inactive; see line 3 in the Abstract; column 3 lines 26-52). Such a filler is similar to other prior art sterile cosmetic fillers such as, for example, compositions based on collagen, hyaluronic acid or calcium hydroxylapatite (examples provided below).

In sharp contrast, the present invention utilizes a biologically-active filler which is based on proliferating cartilage-producing cells. Use of actively proliferating cells in a cosmetic filler is both novel and inventive and represents a departure from prior art cosmetic fillers and from cosmetic fillers currently utilized in cosmetic repairs. The use of actively proliferating cartilage producing cells presents substantial advantages over prior art fillers such as cartilage paste, collagen, hyaluronic acid or calcium hydroxylapatite. Accordingly, the cultured isolated cells of the present invention are capable of integrating with the treated skin tissue without disturbing the

blood supply and without producing unwanted subcutaneous calcified cartilage. By virtue of their proliferative qualities, cartilage producing cells are capable of self-filling skin tissue depressions to the point of contact inhibition while maintaining viability and wrinkle smoothing qualities over an extended period of time. Contact inhibition will prevent over-filling of the defect thus preventing formation of skin bumps (see page 12 lines 7-12 of the instant application). As such, the biological filler (cartilage producing cells) of the present invention is substantially advantageous over traditional sterile fillers in that it is capable of substantially reducing the chances of the wrinkles or rhytids returning, while preventing the possibility that depressions become unsightly bumps (see page 12 line 21 to page 13 line 1 of the instant application).

With respect to Brittberg *et al.*, Applicant wishes to point out that this reference teaches use of cartilage producing cells for the purpose of repairing damaged cartilage tissue, and thus relies upon a function of these cells which has not been correlated with cosmetic repair of skin contour irregularities. More particularly, Brittberg *et al.* teach transplanting cartilage producing cells directly into a site of damaged cartilage tissue for the sole purpose of engrafting and generating new functional cartilage tissue in the treated site. Since Brittberg *et al.* describe a natural site of implantation which leads to engratfment and cartilage formation, they do not provide motivation for an ordinary person skilled in the art to consider a non-natural site of implantation, i.e., subcutaneous, in order to improve skin aesthetics.

In addition, it should be noted that U.S. Pat. No. 4,469,676 teaches against the present invention by using sterilized non-proliferating, non-functional cells. The fact that U.S. Pat. No. 4,469,676 and all other prior art cosmetic repair approaches teach the use of biologically inactive fillers, implies that the ordinary skilled artisan would not consider using viable proliferating cells for repairing skin contour irregularities.

The premise that these references would not motivate an ordinary skilled artisan to use proliferating cartilage-producing cells in cosmetic repair is further supported by the state of the cosmetic repair field in the years that have past since Brittberg *et al* was published in 1994. Since then, research and development in non-surgical cosmetic treatment has been intensive and rapidly growing far outpacing research and development in surgical cosmetic procedures (American Society for

Aesthetic Plastic Surgery statistics http://www.findarticles.com/p/articles/mi m0HMW/is_3_7/ai_115492883). While several new filler products have been developed during the past decade (e.g., Restylane™, Fasciane™, Rediance™, Hylaform™) none include actively proliferating functional cells, clearly showing that the combined teachings of U.S. Pat. No. 4,469,676 and Brittberg *et al* did not motivate the ordinary skilled artisan to utilize isolated cartilage producing cells in cosmetic skin repair.

Thus, it is Applicant's strong opinion that the teaching of Brittberg *et al.*, would not motivate the ordinary skilled artisan to modify the method of U.S. Pat. No. 4,469,676 to utilize proliferating cartilage-producing cells in cosmetic repair of skin contour irregularities.

The Examiner has rejected claims 5 and 6 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 4,469,676 and Brittberg *et al.* and further in view of Atala *et al.* (J. Urol. 150: 745-747, 1993).

The Examiner asserts that the combination of U.S. Pat. No. 4,469,676 and Brittberg *et al.* teach using chondrocytes to treat facial irregularities. Brittberg *et al.* specifically teaches using chondrocytes isolated from the subject. However, Atala *et al.*, teaches that chondrocytes isolated from a different species can be safely injected into a subject in order to produce cartilage. The Examiner therefore asserts that a person of ordinary skill in the art would be motivated to use chondrocytes from a synergic or allogenic source in the skin treatment method taught by the combination of U.S. Pat. No. 4,469,676 and Brittberg *et al.*

As argued above, Applicant believes that a person of ordinary skill in the art could not have been motivated by Brittberg *et al.* and U.S. Pat. No. 4,469,676 to cosmetically repair skin-contour irregularities using cartilage-producing cells.

As further argued in detail in our previous response to Office Action (dated March 15, 2004) Atala *et al.* teach the use of a biodegradable polymer embedded with chondrocytes, which is clearly distinct from the support-free suspension of cartilage-producing cells of the present invention, thereby in fact, teaching against use of free chondrocytes.

Hence, clearly, a person of ordinary skill in the art could not have been motivated by the combined teachings of Atala *et al.*, U.S. Pat. No. 4,469,676 and

Brittberg *et al.* to treat skin contour irregularities with a suspension of cultured isolated cartilage-producing cells.

In view of the above arguments it is respectfully submitted that claims 1 and 3-8 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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